FEATURE

Packaging Matters — Part I: Design of the Pack

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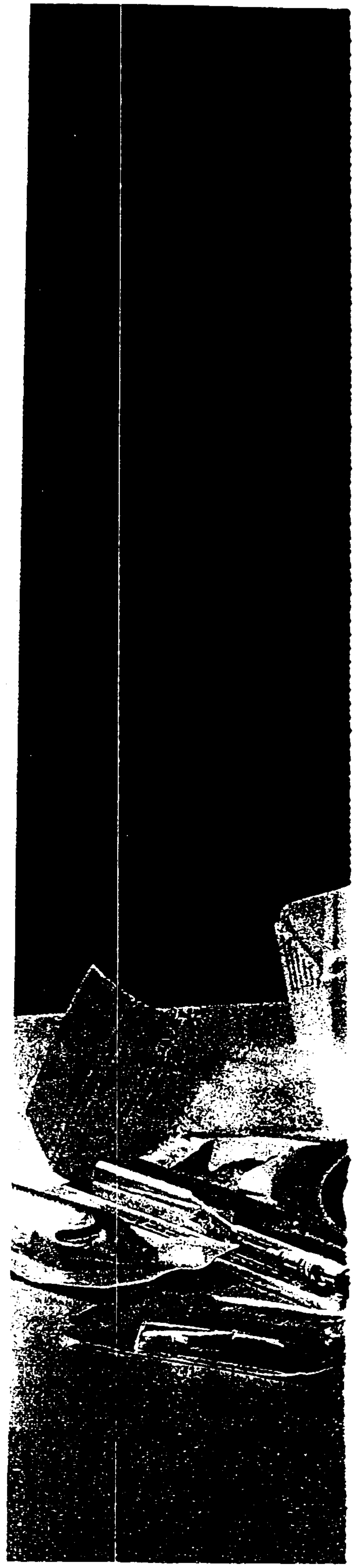
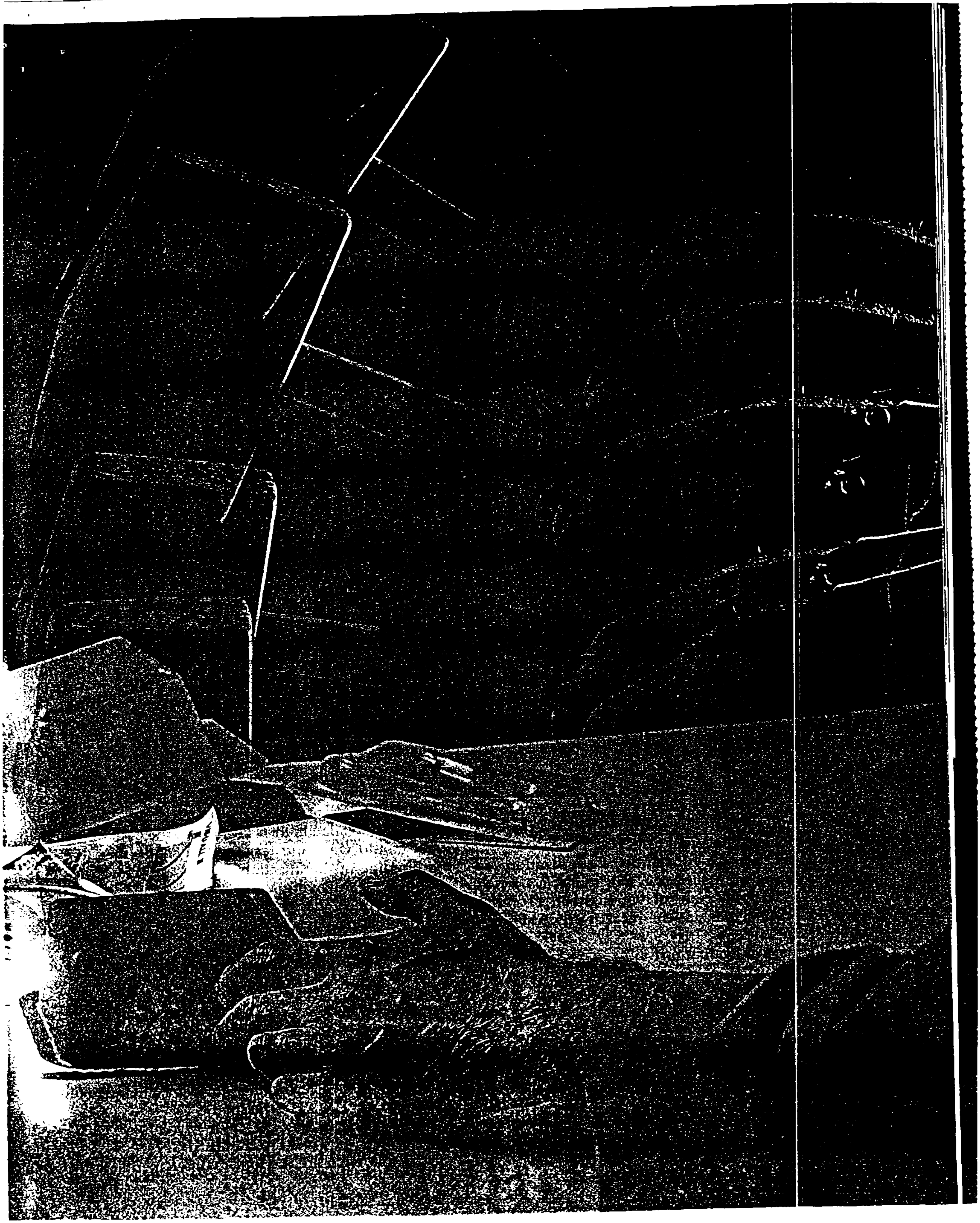


Following the author's discussion of seals and seal integrity in medical packaging in the May/June issue of Medical Device Technology, _this article discusses the parameters involved in the design of a pack. These parameters are discussed in relation to each integral part of the overall medical device package, from the inner pack to the shelf pack, and the conclusion is reached that a number of pitfalls could be avoided if the device and the package were designed together. Part II will deal with material selection._

INTRODUCTION

If the medical device industry heeded its own recommendations, there would be no need for this article.



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In March 1981, the Medical Disposable Sterile Packaging Association (MEDISPA) — now under the banner of the European Confederation of Medical Device Suppliers Association (EUCOMED) — published its recommendations for packaging and labelling. These recommendations cover all the problems that are likely to face those working in the field of medical packaging, yet I have not once seen this document on a packaging engineer's desk. The checklist for pack design in MEDISPA's recommendations covers such areas as

- confirmation of the suitability of a material for preconditioning and sterilization,
- microbiological challenge tests,
- label application to withstand the sterilization process and long-term storage,
- features of the pack material that might affect or damage the product, such as chemical or physical migration of constituents,
- journey hazard evaluation
- aseptic removal,
- stability for handling and palletization, and
- providing space for clear labelling with batch-number bar code and instructions for use.

This approach can result in numerous problems, such as

- incorrect material choice,
- poor pack design,
- incorrect package sealing and machine choice,
- initial sterilization failures/damage,
- delayed product launch, and
- inflated costs.

Such problems can be avoided if the pack and the device are designed and developed at the same time. For example, handling and sterilization of the pack at the prototype stage in the development of the medical device could highlight weak points in the outer shape of the package or detect *dead spots* during the sterilization cycle.

Sterilizing a handful of products in a tray is very different from sterilizing a complete pallet load of inner-wrapped and outer-packed products where orientation on the pallet and in the sterilizer can have varying effects. (See Figures 1 and 2.) The *full* pallet must be imitated by mocking up one complete carton unit and stacking this in the most vulnerable position on a pallet with simulation of both weight and surrounding characteristics.

This article attempts to show how the combined development of package and device can save both time and money. Product design has a major effect on pack design and the gauge of material required for the package. Injection mouldings, for example, should be viewed in relation to their position in the packs and general mould wear and tear, such as split lines (the dividing line of the injection mould) and injection sites wearing and leaving sharp ridges or high spots that can protrude and cause surprising damage to the packaging materials over time.

Also, by performing transit tests at the earliest possible opportunity, those areas of the product that are likely to be problematic in relation to the package will be highlighted, such as push-fits of connectors that can become loosened, and exit angles of connectors into coiled tubing that can push against the blister lid during sterilization and cause excess pressure on the seal

[illegible] such as suction catheters, packaging costs are frequently on a par with the device costs, the time spent on the design and testing of the pack is often limited and left until the product design has been completed.

THE PACK DESIGN

The following are the four main elements of the device pack:

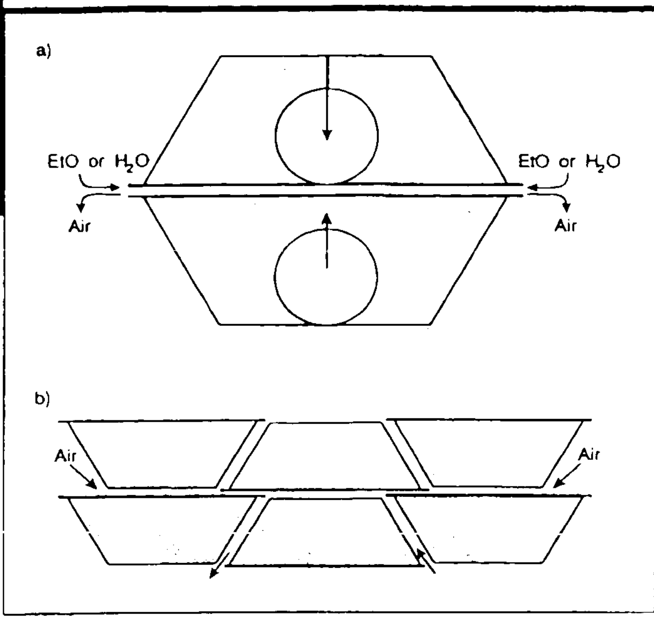


Figure 1: *Blister orientation. a) Placing of permeable lid directly against permeable lid reduces flow of air and sterilant. Escaping air seals lids together. b) Pathways around blister packs allow for easier flow of air and sterilant.*

- Inner pack: used for devices that require a double pack, such as operating-theatre devices. Inner packs generally take the form of a smaller copy of the unit container, such as a blister inside a blister, pouch inside a pouch, or a polyethylene or glassine bag.
- Ancillary components: those components that are packaged with the device, such as backing card, preformed supports, needle guards, leaflets, or inserts.
- Unit/sterilization container: the main package containing an individual device or number of devices that together make up a procedural kit. This pack must maintain the sterility and integrity of the contents until they are used. It must also permit aseptic removal of the contents and, once opened, must not be resealable.
- Shelf/multiunit container: this is the package containing a number of unit containers and offering physical protection during the normal life cycle of the device.

INNER PACK

Because this part of the pack is considered sterile, it is normally kept in place until just before the device is used. The inner pack should facilitate easy and con-

desirable, and a smaller version of the unit blister pack or pouch is considered the ideal design.

When polyethylene bags are used as inner packs, the bag frequently sticks to the device. This can be coun-

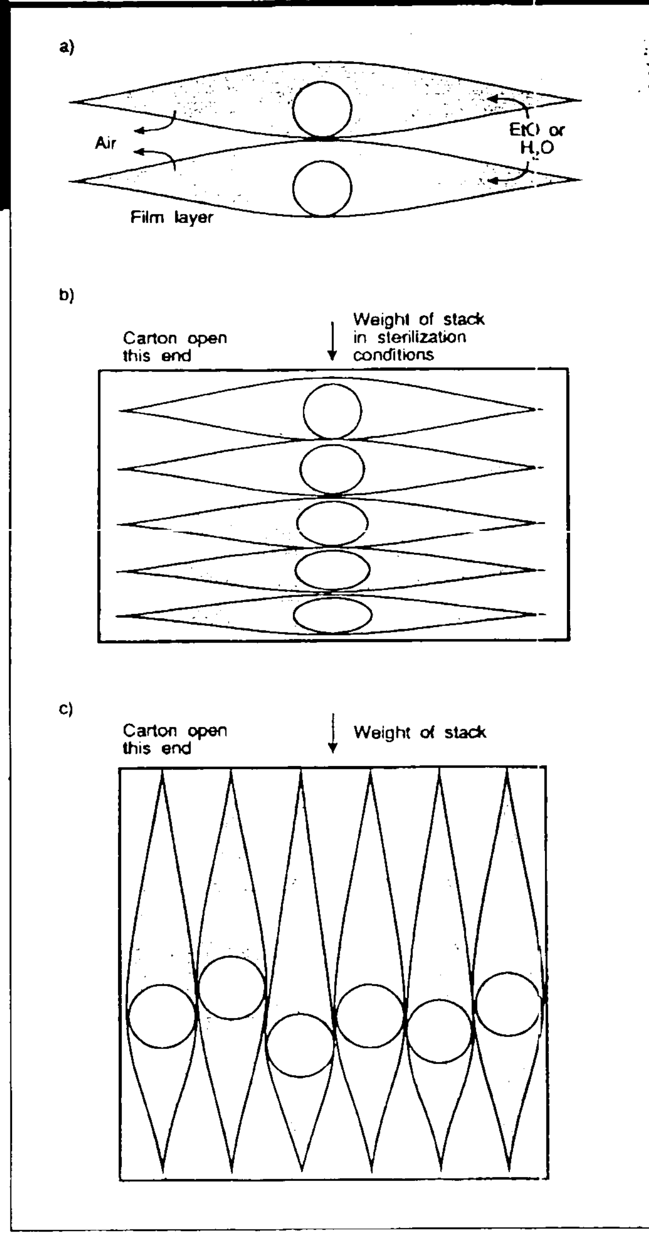


Figure 2: *Pouch orientation in carton and sterilizer alters pressure points on products. a) Permeable layers in contact do not obstruct flow because of ballooning pushing packaging apart. b) Cartons stacked vertically with products directly one over another can cause distortion in warm or hot conditions when plastic is soft. c) Products packed and stacked on edge protect each other.*

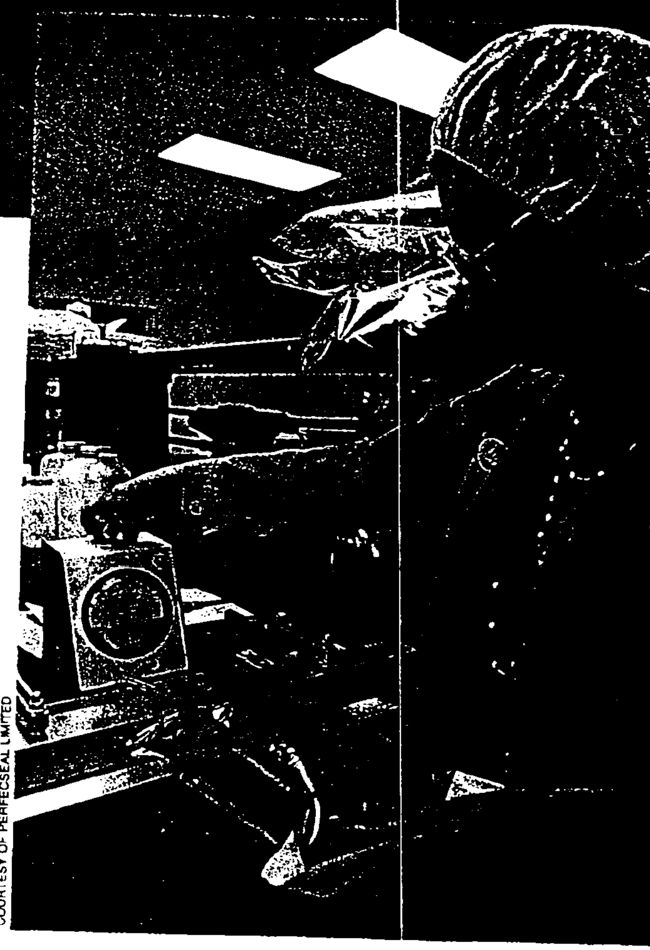
tered by using a suitable gauge of polyethylene that pro-

ANCILLARY COMPONENTS

Some ancillary components are required for the protection of delicate parts of a medical device, such as spe-

cialized catheter tips that are often protected through the use of formed-plastic inserts or insert cards. The great difficulty in respect of such protective components is finding a suitable and foolproof means of holding the device without causing it damage.

Channels with undercuts are generally used with the formed plastic, and holding flaps can be introduced into the insert card if they are made of a suitable and nonshredding material. All manner of needle guards have been used — from injection mouldings to both straight and ribbed extruded tubing.



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UNIT/STERILIZATION CONTAINER

The design of the unit/sterilization container takes most of the time and energy of the packaging engineer, as material or seal failure in this container can lead to loss of sterility. The unit container also carries the device manufacturer's quality image into the hospital and operating theatre. Confidence with the product's condition and success in its use is set by the initial pack appearance, its feel, and its function during the opening process.

There are three elements in the unit/sterilization container:

- blister pack: a thermoformed tray with sealed liddings;
- peel pouch: consisting of two components — a film front and a paper or Tyvek back; and
- polyethylene bag, breather bag, or patch bag: either a straightforward polyethylene bag with a tear-open feature; a specialized polyethylene bag made from two webs welded at the side and sealed to a peel strip of Tyvek; or a polyethylene bag with Tyvek disks sealed over holes to allow for gas sterilization, with a tear-open weak line built in.

Blister/thermoformed pack. The reduced volume of the three-dimensional blister pack when compared with the pouch pack makes it appear very attractive to both marketing personnel and hospital administrators who are very conscious of the necessity to save shelf space. However, there are a number of disadvantages associated with the use of this type of package, such as

- production speeds approximately 25–30% slower [illegible]
- [illegible]
- greater personal skills needed for the thermoforming "art";
- greater care required when sealing porous lidding materials in order to produce a clean peel with adhesive-coated materials or minimal fibre lift with uncoated materials;
- heat having to be applied to the lidding surface, which creates the possibility of the sealant layer melting too far into the porous material, resulting in weak seals or material breakdown during the peeling operation.

The last of these requirements applies equally to an adhesive coating on the lidding material or to an uncoated material that relies on the polyethylene or polypropylene layer of the thermoformed web as the sealant. The result with nonporous materials can be a squashing effect that effectively reduces the seal strength.

If the volume of the pack is reduced to a point where the product can push against the lid as the packs come out of the sealing head, the lidding can be pushed away from the seal flange, causing separation because [illegible]

[illegible]

There are particular disadvantages associated with using paper lidding material, especially when this material is uncoated. The pack can become orientated in such a way that the main peel operation becomes

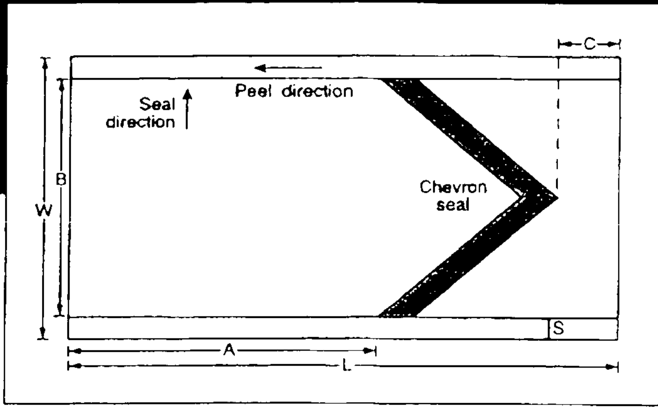


Figure 3: *Schematic representation of pouch pack where A = internal length, L = overall length, B = internal width, W = overall width, C = peel flap, and S = seal width.*

aligned with the cross direction of the paper lid. When uncoated paper is used, seals made in the cross direction are weaker than those made in the machine direction. Seal checks also need closer attention, although this need is not so great when Tyvek-film lidding is used, even though seal strengths have still been found to be different.

When gas or steam sterilization is used, permeability of the lidding material is of paramount importance in order that the easy evacuation of air and permeation of the sterilant be permitted. The blister pack has a comparatively small porous lid-to-pack volume compared to the pouch, which can increase strain on the seals and cause ballooning as the air is evacuated. Checking the evacuation rate from the pack — by testing mock-ups in an evacuation chamber — is a vital part of pack design, as long as test conditions are as realistic as possible. Testing a single layer of packs is useless; it is far better to put the packs in a carton or similar confined space that replicates production conditions as closely as possible.

Self-adhesive labels can reduce permeability quite considerably, especially when the CEN recommendations for multilingual information necessitate an increase in the size of such labels.

Too close a contact between a highly-plasticized device, such as a cuff or balloon, and an unplasticized tray can also cause problems. Contact over a five-year shelf-life can cause migration of the plasticizers and a subsequent loss of flexibility.

Male forming of preformed semirigid trays causes [illegible]

[illegible] access via a peeled lid at the time of use while remaining intact during a punishing sterilization process and a storage period of up to five years. During its life cycle, the atmosphere around the pack is likely to change from hot to cold, causing expansion and contraction of the air contained within it; variations in external pressure can also occur when the store cupboard or packing drawer is closed, and loading accidents —such as the accidental dropping of a pallet — can push the product against the seal.

Whenever possible, thermoformed trays should be female moulded, with clamps around the proposed seal flanges. This will ensure that the flanges remain the same gauge as the original material and will give some chance of achieving uniform seals. Peel tabs must be of a size and shape that allow a quick and easy grip by users who are wearing gloves and who are frequently in a hurry. It is therefore important to consider the effect of sharp corners or a change in peel direction; the need to apply a higher peeling force may result in the product flying out of the pack when it is opened.

Shrinkage of the plastic web after forming can lead to the pack becoming distorted after separation from the web — a frequent occurence that can also interfere with ease of peeling and adversely affect the quality of the seal.

From the above, a list of parameters that need consideration when designing a thermoformed pack can be produced:

- Product support (if necessary).
- Sterilization method: does the lidding need to be gas permeable, high-heat resistant, or radiation resistant?
- Tool design for forming the tray: female is preferable to male, and vacuum, pressure, and plug-assist methods are all suitable. A sealing system should be chosen that ensures easy peeling and a uniform seal.
- Likely transit and storage method.

Overall, the blister pack is an efficient and effective method of packing, as long as the time cost and the customer are always considered.

The pouch pack. The choice of pouch packs is between those produced on premade pouch-filling lines and those produced on packing machine form-and-fill systems. (See Figure 3.) The ultimate decision as to which system should be used is generally made on the [illegible]

[illegible] product changes, and the capital cost of the system is low. The system can accommodate smaller pack sizes, especially smaller pack widths, than those accommodated by the machine form-and-fill system, but throughput is slow. By comparison, the capital cost of

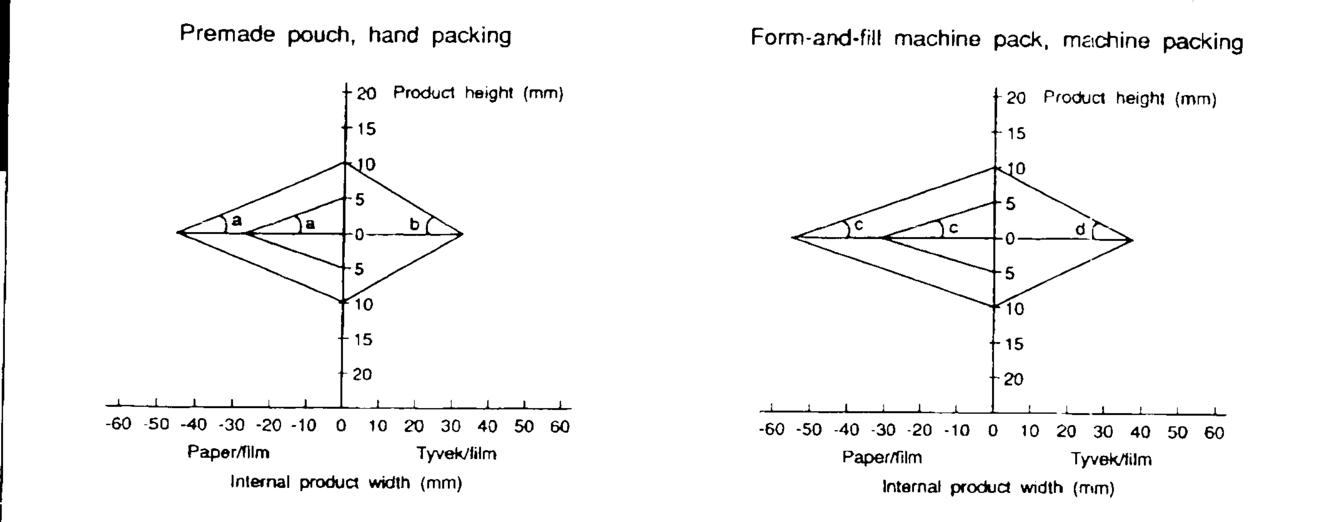


Figure 4. *Guidelines for dimensions of premade pouch and form-and-fill machine pouch. A = 13°, B = 17°, C = 11°, and D = 15°.*

machine form-and-fill systems is high; changeover between products is slow, but throughput is fast.

Consequently, for multi-product-size, low batch-size packaging conditions, the premade pouch can be effective. Packing lines can be streamlined with air-assisted opening and rotary-sealing functions. The premade pouch is less effective, however, for a single-pack size with runs of approximately 2 m/annum, in which case the machine form-and-fill system becomes more effective.

Figure 4 sets out guidelines that can be used when undertaking cost estimates, machine estimates, or when preparing sample packs before the product development engineer has produced a product mock-up. The pouch length can be assessed in order to give the same distance between product and cross seals. The dimension can be used for paper weight between 59 gm^{-2} and 100 gm^{-2}, coated or uncoated, and Tyvek weighing 61–75 gm^{-2}, coated or uncoated.

The difference between coated paper and coated Tyvek reflects the contrast between the adhesive coatings that can be used on these two materials; Tyvek displays a far stronger bond than paper if the correct adhesive coating is used. A similar difference can be seen with latex reinforced paper.

The difference in material weight within the same substance category affects the burst-strength and tear-strength levels of a package, therefore allowing for heavier weights and larger packs with the same seal

and fill pouches. It is essential to keep a balance between the two webs, and the stiffness of the film layer should respond to the stiffness of the paper or Tyvek layer.

The pouch should always be designed so as to allow it to be peeled open from both webs with equal force because if the film side is made flimsier than the paper side, the peeling force will be biased and will affect the angle of peel. Measurement of the same seal at varying angles should show that the nearer the person opening the pack can get to achieving a 90° separation angle, the easier it is to open and the less likelihood there is of tearing the paper surface or causing fibre lift. This problem doesn't occur with Tyvek sealed to film.

The tendency to seal down the peel flap is a source of constant irritation to users and can be controlled with inspections and suitable specification controls for machine settings. The peel flap is frequently made smaller as the pouch size reduces, but packaging engineers should remember that the end user remains the same size and often has gloves on.

The peel strength of long, narrow pouches should be reduced relative to wide, rectangular pouches. This can be done by reducing the seal width, bearing in mind that the minimum seal width required for a grid-patterned lacquer must allow for at least two lines of adhesive. Allover coatings can be tailored more closely. Peel strength versus seal strength is also an important consideration in respect of sterile pouches and should be engineered in such a way as to suit both the sterilization stresses and the mechanism of opening.

The edge of the seal is frequently stronger than the main body of the seal due to sharp right angles on the

al strength from internal strain. Very wide pouches do not offer this advantage so readily. (See Figure 5.) This can lead to excessive effort when initiating the peel, followed by a jerky response with the follow-on.

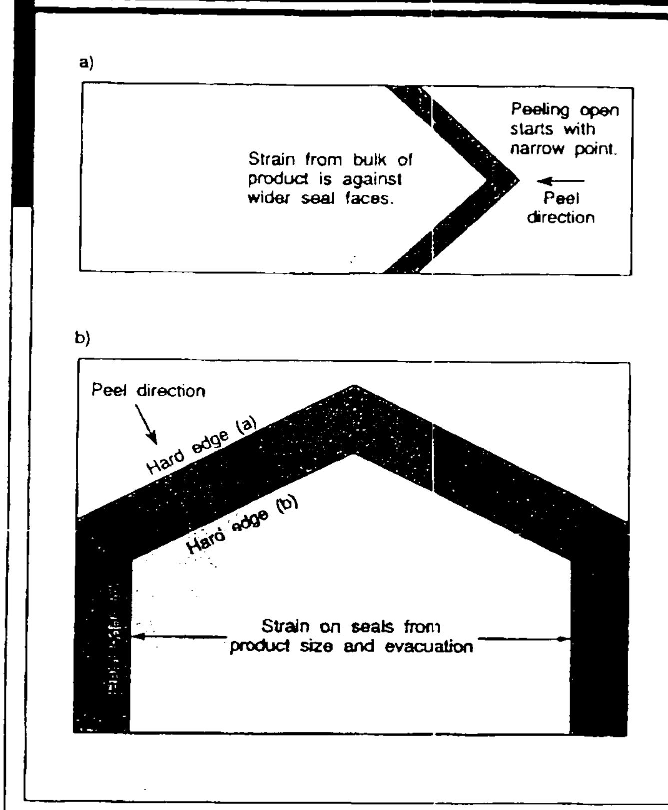


Figure 5: *a) Schematic representation of chevron lead-in. b) Schematic representation of chevron lead-in on wide pouch. Hard edge (a) causes difficulty at initiation; hard edge (b) can cause fibre lift when seal strength is above level of fibre tear; hard edge (c) can be beneficial against strain from product or evacuation.*

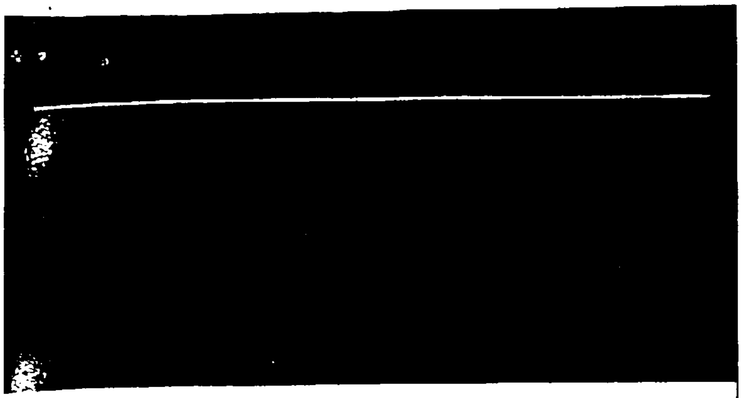
The trailing or inner edge of the cross seal can produce the same jerking effect as the seal opens. The level of seal can overcome the mechanical strength of paper fibres and lead to tear or fibre lift, a solution being to round off the profile edges of cross seals. Side seals, on the other hand, can benefit from a stronger edge to the seal, as this is the direction of strain exerted by the bulk of the product or by the ballooning effect during evacuation.

The bag pack. The straightforward polyethylene bag used for the packaging of garments and drapes is traditional and inexpensive, but the opening techniques for the user are not always satisfactory.

The weak or stressed line across the bag is very difficult to engineer in such a way that the same degree of force is required for opening from bag to bag, and the snap-top effect needs practice and leaves a nonsterile

and the easy to open peel pouch. The advantages of this kind of pack are threefold.

- bulky items can be held in tight packs because the side seals are welded,



- the opening technique is the same as for a pouch (i.e., peeling from a flap), and
- when the peel flap is removed it exposes the product, which can be extricated without contamination from nonsterile surfaces.

The packing technique for bags can be improved and quickened by the use of a bag-opening system such as the About Packaging Pouchmaster PacSystem (Acorn Equipment, Stanmore, United Kingdom) already used in the medical device field. Packaging units can also be set up that produce light airflow to open the bag, which can frequently be the lengthiest activity with polyethylene bags. Excess material is removed when the bag is sealed.

THE SHELF/MULTIUNIT CONTAINER

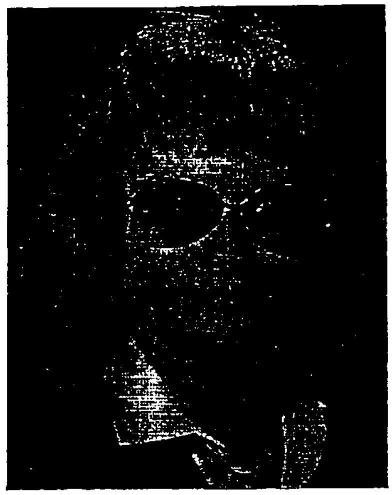
The cartoning of medical devices appears to have turned full circle between the 1970s and the 1990s. In the 1970s, cartons tended to be made from white-lined chipboard or other forms of glossed, folding boxboard to give at least the appearance of cleanliness and sterility. The late 1970s and the early 1980s saw the introduction of "E" Flute corrugated board designed to provide better support and lower cost. Device cartoning in the 1990s is dominated by "E" Flute, but price increases have been so great as to once again make chipboard more economical and, therefore, more attractive.

Whichever material is used, the carton must protect and inform. It must protect the product and unit pack through sterilization and during a five-year shelf-life. It must inform the hospital personnel of its exact contents, the manufacturer's details, the batch-tracing numbers, and the date of expiry; and it must assist storeroom personnel by allowing easy stacking and removal of the product.

There are a number of guidelines in relation to cartoning medical devices that should be considered: pack from the wide side because it is quicker and easier; dispense through the narrow side; store with the smallest dimension along the shelf; and stack on the ends so the board is at its strongest. ■

STAFF EXPANSION

Medical Device Technology's Director of Regulatory Affairs



Aster Publishing Corporation and *Medical Device Technology* are pleased to announce that Doris J. Bates, PhD, has joined the company as Director of Regulatory Affairs. In this capacity, Bates will act as a staff consultant and adviser, drawing upon her seven years of experience in the pharmaceutical industry. In addition, she will actively contribute to meeting our readers' needs for timely information concerning developments in regulatory affairs, clinical research, and related areas. Bates received her BS in Biochemistry in 1977 from the University of Maryland, College Park, Maryland; her MA in 1979 from Brandeis University, Waltham, Massachusetts; and her PhD in Organometallic Chemistry in 1984 from Brandeis.

Beginning in 1983 as senior scientist/scientific writer at Sandoz Pharmaceuticals in East Hanover, New Jersey, Bates was responsible for reviewing and editing drug master files and INDs (focusing on chemical synthesis, structure proof, and analytical controls). Later, as manager of technical operations coordination at Sandoz, Bates was responsible for reviewing, submitting, and following up chemistry, manufacturing, and controls-related supplemental submissions, as well as reviewing the chemistry sections of original NDAs, ANDAs, and AADAs and working extensively with DMFs and VMFs.

In 1988 Bates joined Bristol-Myers in Syracuse, New York, as manager of chemistry/pharmacy regulatory affairs. She was responsible for producing, reviewing, submitting, and following up the chemistry, manufacturing, and controls sections of INDs, IND amendments, IND annual reports, NDAs, and NDA amendments, as well as CTA, CTX, and PLA submissions in the United Kingdom.

In 1989 Bates moved to Fisons in Rochester, New York, as senior manager of international regulatory affairs. This move involved a six-month assignment in the firm's Loughborough, U.K., office, where Bates was active in international clinical trials applications and PLAs, primarily involving EEC and EFTA countries. On her return to the United States, she

...clinical matters and progressing to international matte... make her a valuable resource for the Editorial and Conference divisions of *Medical Device Technology*.

—*The Editor*